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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/292,056	04/14/99	GREENBERGER J	PITT-1DIV

HM12/1005

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EXAMINER	
SOUAYA, J	
ART UNIT	**PAPER NUMBER**
1655	11
DATE MAILED:	10/05/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/292,056	Greenberger et al
Examiner	**Art Unit**
Jehanne Souaya	1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jul 26, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1 and 47-123* is/are pending in the application.

4a) Of the above, claim(s) *65-69, 71-73, 82-85, 101, 102, and 105-113* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 47-64, 70, 74-81, 86-100, 103, 104, and 114-123* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 7

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Election/Restriction

The claims for groups I-VI and IX have been rejoined. Accordingly, an action on the merits follows for claims 1, 47-64, 70, 74-81, 86-100, 103, 104, and 114-123.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 57, 74, 80, 86-88, 90, 93, 99, 100, 114, 115, and 118-123 are rejected under 35 U.S.C. 102(b) as being anticipated by Maruhashi *et al.* (U.S. Patent 5,403,735 (Apr. 4, 1995)).

Maruhashi teaches a method and apparatus for culturing and detecting cells (abstract). Maruhashi teaches that prior art methods of testing a cell culture for cell viability, growth rate or other diagnostic means have the disadvantages of requiring the opening of a closed and sterile culture system to test, liquid used for testing cannot be returned to the culture because of stains used to test viability, and that such staining means are not very reliable and do not provide any information as to the ratio of viable cells (col. 2 line 48-col. 3 line 12). Maruhashi teaches means for culturing and observing cellular cultures where the means for culturing and means for detecting are in fluid communication so that the culture system does not need to be opened and

where microscopy is used to detect cell division state, thereby obviating the need for staining or culture sampling (col. 8 lines 36-67 & Fig.s 1, 4 & 8). Maruhashi teaches that such a system can include a temperature controller, pumps and injectors to maintain the pH, temperature, osmotic pressure, dissolved oxygen (col. 7 line 64-col. 8 line 5, col. 16 lines 18-45& Figure. 21 & 23). Maruhashi teaches that the microscope is in communication with a television camera to capture images and an image processing and calculating device (i.e. computer; see col. 8, line 67-col. 9 line 11). Maruhashi teaches that two microscopes, camera and data processor setups can be used simultaneously (Figure. 8). Maruhashi teaches a cell culture system (Figure 21 and col. 16, lines 18-52) where an image pick up device (e.g. a microscope (509)) is linked to a controller (510) and is directly attached to the culture vessel (506). Maruhashi teaches that the image pick up device (509) operates as describe for other embodiments of the invention and describes (509) as monitoring the cells and microscopic small particles (col. 16, lines 35-40). Therefore, the teachings of Maruhashi as to a method and apparatus for monitoring cell activity by using a culturing and testing system in fluid communication where the temperature and pH of the culture is regulated and the testing system comprises a microscope, television camera and data processor and where the cells are examined in the location in which they are grown, anticipates all of the limitations of the instantly claimed invention.

3. Claims 57 and 74 are rejected under 35 U.S.C. 102(e) as being anticipated by Shuler *et al.* (U.S. Patent 5,612,188 (Mar. 18, 1997;effective filing date May 24, 1993)).

Shuler teaches a system for culturing and detecting cell characteristics (abstract). The apparatus and method of Shuler comprises multiple compartments so that different cell samples or different drugs or cellular metabolites or different concentrations of drugs or cellular metabolites can be tested simultaneously (col. 2 lines 39-47 & col. 3 lines 17-42). Shuler teaches that the multiple culture chamber can be kept in a larger chamber with ports for injection and removal of culturing media (Figure. 5). Shuler teaches that such a biochamber can be in fluid communication with the detection system (Figure. 6). Shuler teaches that on-line detection of culture media can be conducted by numerous means (col. 6, lines 60-67). Shuler teaches that the temperature and culture components, such as oxygen and carbon dioxide are monitored and regulated (col. 7 lines 36-43). Therefore the teachings of Shuler anticipate all of the limitations of the instantly claimed invention by teaching a method and apparatus for holding, culturing and determining the state of cells where multiple samples are cultured and analyzed.

4. Claims 57, 74, 80, 86-88, 90, 93, 99, 100, 114, 115, and 118-123 are rejected under 35 U.S.C. 102(b) as being anticipated by Matsuzaki *et al.* (U.S. Patent 5,162,204 (Nov. 10, 1992)).

Matsuzaki teaches a method and apparatus for culturing and detecting under conditions where the detecting step is performed under the physiological conditions of the culturing step, the detection portion of the apparatus is in fluid communication with the culturing portion (abstract, col. 1 lines 11-15, lines 60-65). Matsuzaki also teaches (col. 9 lines 17-24 and Figure 11) that the observing or detecting portion (4') of the apparatus may be an integral portion of the culturing

vessel ((1); i.e. place where cells are grown). Matsuzaki teaches that this system has the advantage of not exposing the culture to external conditions during the detecting step, the culture used for detection can be returned to the culturing vessel, and that information obtained from the detecting step can then be used to effect changes in the composition of the culture thereby enhancing culturing efficiency (abstract, col. 2 lines 31-36 and 43-45 & col. 3 lines 13-15). Matsuzaki teaches that the use of a microscope for the detection of the culture and a digital processor (i.e. computer) to processes the images (col. 5, line 63-65 & Figure. 14). Matsuzaki teaches that the temperature, pH and dissolved oxygen and carbon dioxide conditions of the culture are monitored and controlled (col. 8 line 65-col. 9 line 5, Fig.s 5 & 12). Therefore, Matsuzaki anticipates all of the limitations of the instant claims by teaching a method and apparatus for culturing and measuring cell conditions where the culturing and measuring components are in fluid communication and a microscope and data processor are used to detect the cells and where the state of the cells is detected in the vessel in which the cells are grown. It is noted that the claimed subject matter drawn to a method of holding cells merely recited that two cells are measured and does not impose the limitation the cells are obtained from separate compartments.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1, 47-56, 58-64, 70, 75-79, 81, 89-92, 94-98, 103, 104, 116, and 117 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Maruhashi et al (U.S. Patent 5,403,735 (Apr. 4, 1995) and Weinreb et al (US Patent 5,310,764) in view of Shuler *et al.* (U.S. Patent 5,612,188 (Mar. 18, 1997;effective filing date May 24, 1993)).

Maruhashi teaches a method and apparatus for culturing and detecting cells (abstract). Maruhashi teaches means for culturing and observing cellular cultures where the means for culturing and means for detecting are in fluid communication so that the culture system does not need to be opened and where microscopy is used to detect cell division state, thereby obviating the need for staining or culture sampling (col. 8 lines 36-67 & Fig.s 1, 4 & 8). Maruhashi teaches that such a system can include a temperature controller, pumps and injectors to maintain the pH,

temperature, osmotic pressure, dissolved oxygen (col. 7 line 64-col. 8 line 5, col. 16 lines 18-45& Figure. 21 & 23). Maruhashi teaches that the microscope is in communication with a television camera to capture images and an image processing and calculating device (i.e. computer; see col. 8, line 67-col. 9 line 11). Maruhashi teaches that two microscopes, camera and data processor setups can be used simultaneously (Figure. 8). Maruhashi teaches a cell culture system (Figure 21 and col. 16, lines 18-52) where an image pick up device (e.g. a microscope (509)) is linked to a controller (510) and is directly attached to the culture vessel (506). Maruhashi teaches that the image pick up device (509) operates as described for other embodiments of the invention and describes (509) as monitoring the cells and microscopic small particles (col. 16, lines 35-40).

Although Maruhashi does not teach an apparatus where each individual cell can be examined while the cells remain in place in a location in which they are grown, Weinreb et al teach an apertured cell carrier where each individual cell has a specific defined address within the carrier so that each individual cell can be monitored (see abstract). Weinreb teaches that an object of their invention is to provide a process for multiplying cells located within the holes of the cell carrier. The apparatus of Weinreb contains holes in an array where each hole which contains an individual cell is known and is identifiable (see col.4, lines 14-15). Weinreb teaches that one can subject all of the cells to one or more tests, but can examine the properties of each cell by directing the particular diagnosing/ measuring instruments to the cell's unique address (col.4, lines 34-39). Weinreb further teaches that the apparatus includes a device for aligning the carrier with a device whereby the individual addresses of the holes in the carrier are identifiable by a set of x

and y coordinates as when the carrier is viewed through a microscope (col.11, lines 50-55). Weinreb also teaches that an orifice (150) is connected by an outflow tube (160) to a pump (162) where the pump serves to produce a pressure differential across the carrier which pulls the cells into the apertures of the carrier. Weinreb teaches that a basin (156) is configured so as to allow a microscope objective to be brought close enough to the carrier to bring the apertures into focus. Weinreb teaches that solutions are provided to the basin by one or more inflow tubes with are connected to syringe needles. The inflow tubes are used to introduce bathing and reagent solutions to the cells.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to include the embodiment in the apparatus of Maruhashi that each cell be examined as Weinreb teaches an apparatus that enables the address of each cell to be known so that each cell can be identified and monitored and teaches that the cells in each hole may be multiplied. The ordinary artisan would have been motivated to modify the apparatus of Maruhashi to be able to monitor each individual cell as in the apparatus of Weinreb because Weinreb teaches that a cell by cell analysis provides more information for the understanding of biological implications and makes it possible to realize such analysis very quickly and accurately (see col.6, lines 58-63). Therefore, the combined teachings of Maruhashi and Weinreb as to a method and apparatus for monitoring cell activity by using a culturing and testing system in fluid communication where the temperature and pH of the culture is regulated and the testing system comprises a microscope, television camera and data processor and where the cells are examined in

the location in which they are grown, with the motivation taught by Weinreb to provide an apparatus wherein each individual cell can be monitored, teach the embodiments of the instantly claimed invention.

As discussed, the combined teachings of Maruhashi and Weinreb teach a method and an apparatus for monitoring cell activity by using a culturing and testing system in fluid communication where the temperature and pH of the culture is regulated and the testing system comprises a microscope, television camera and data processor and where the cells are examined in the location in which they are grown, where each individual cell can be monitored. Although Maruhashi and Weinreb do not teach an apparatus where *different* concentrations of metabolites or drugs can be tested simultaneously, Shuler teaches a system for culturing and detecting cell characteristics (abstract). The apparatus and method of Shuler comprises multiple compartments so that different cell samples or different drugs or cellular metabolites or different concentrations of drugs or cellular metabolites can be tested simultaneously (col. 2 lines 39-47 & col. 3 lines 17-42). Shuler teaches that the multiple culture chamber can be kept in a larger chamber with ports for injection and removal of culturing media (Figure. 5). Shuler teaches that such a biochamber can be in fluid communication with the detection system (Figure. 6). Shuler teaches that on-line detection of culture media can be conducted by numerous means (col. 6, lines 60-67). Shuler teaches that the temperature and culture components, such as oxygen and carbon dioxide are monitored and regulated (col. 7 lines 36-43). It is noted that the claims recite that the cultures can be viewed, this term has been interpreted to mean that the cultures are visually accessible, as

those of Shuler are and that the term "imaging mechanism" can encompass a visual image or a chromatograph generated from analysis of the contents of the cell culture, as that of Shuler.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the method and apparatus of Maruhasi and Weinreb to provide an apparatus where different concentrations of metabolites and reagents can be tested. Thus the teachings of Maruhashi & Weinreb and Shuler would have permitted the ordinary artisan to have examined, for example the rate at which two distinct cells divided or the effect of a drug or cellular metabolite on cell division, included a test and control culture kept under the same culture conditions where the culturing and detecting are automated. It would have been further prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the method and apparatus of Maruhashi & Weinreb and Shuler so that both growth and quiescent media were available to be added to the cellular cultures so that when, as detected by the automated culturing and detecting system, the optimal growth conditions are achieved, cell division could have been slowed by the addition of a second media. It would have further been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the method and apparatus of Maruhashi & Weinreb and Shuler for detection of changes in the culture media as related to cell growth states to have provided additional information as to the cellular division process because Shuler teaches that the analysis of culture media as an important tool in the study of cultured cells. Therefore the combined teachings of Maruhashi & Weinreb and Shuler teach all of the limitations of the instantly claimed invention by teaching a method and

apparatus for holding, culturing and determining the state of cells where multiple samples are cultured and analyzed.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 1, 51-57, 74, 75, 79, 80, 86, 90, 95, 97, 100, 114, and 115 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-32, 41, and 42 of U.S. Patent No. 6,008,010. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are coextensive in scope.

9. No claims are allowable.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703)308-6565. The examiner can normally be reached Monday-Thursday from 7:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600

Jehanne Souaya
Jehanne Souaya
Patent examiner
Oct. 4, 2001